

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1-47. (canceled)

48. (currently amended) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of, ~~comprising~~ a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 or a perfectly complementary sequence thereof.

49-50. (canceled)

51. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 48 and a promoter, wherein the nucleic acid and the promoter are operably linked.

52. (original) The recombinant expression vector of claim 51, wherein said vector is suitable for transfection of a bacterial cell.

53. (currently amended) An isolated heterologous cell transfected with the vector of claim 51, wherein said cell expresses a biologically active  $\beta$ -secretase.

54. (original) The cell of claim 53, wherein said cell is a eukaryotic cell.

55. (original) The cell of claim 53, wherein said cell is a bacterial cell.

56. (original) The cell of claim 53, wherein said cell is an insect cell.

57. (original) The cell of claim 53, wherein said cell is a yeast cell.

58. (currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleic acid nucleotide-sequence encoding the a beta secretase, wherein the nucleic acid consists ~~consisting~~ of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 or a perfectly complementary sequence thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

59. (original) The method of claim 58, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

60. (previously presented) The method of claim 59, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

61. (original) The method of claim 58, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

62. (previously presented) The method of claim 61, wherein said antibody binds specifically to SEQ ID NO: 43.

63. (canceled)

64. (currently amended) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of ~~comprising~~ a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

65. (original) The cell of claim 64, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

66. (previously presented) The cell of claim 64, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

67. (original) The cell of claim 64, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

68. (previously presented) The cell of claim 64, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

69. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 82.

70-113. (canceled)

114. (previously presented) An isolated nucleic acid, comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 58 or a perfectly complementary sequence thereof.

115. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 114 and a promoter, wherein the nucleic acid and the promoter are operably linked.

116. (previously presented) The expression vector of claim 115, wherein said vector is suitable for transfection of a bacterial cell.

117. (currently amended) An isolated heterologous cell transfected with the vector of claim 115, wherein said cell expresses a biologically active  $\beta$ -secretase.

118. (previously presented) The cell of claim 117, wherein said cell is a eukaryotic cell.

119. (previously presented) The cell of claim 117, wherein said cell is a bacterial cell.

120. (previously presented) The cell of claim 117, wherein said cell is an insect cell.

121. (previously presented) The cell of claim 117, wherein said cell is a yeast cell.

122. (previously presented) An isolated nucleic acid comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 59 or a perfectly complementary sequence thereof.

123. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 122 and a promoter, wherein the nucleic acid and the promoter are operably linked.

124. (previously presented) The expression vector of claim 123, wherein said vector is suitable for transfection of a bacterial cell.

125. (currently amended) An isolated heterologous cell transfected with the vector of claim 123, wherein said cell expresses a biologically active  $\beta$ -secretase.

126. (previously presented) The cell of claim 125, wherein said cell is a eukaryotic cell.

127. (previously presented) The cell of claim claim 125, wherein said cell is a bacterial cell.

128. (previously presented) The cell of claim 125, wherein said cell is an insect cell.

129. (previously presented) The cell of claim 125, wherein said cell is a yeast cell.

130. (currently amended) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of ~~comprising~~ a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: [[43]] 63 or a perfectly complementary sequence thereof.

131. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 130 and a promoter, wherein the nucleic acid and the promoter are operably linked.

132. (previously presented) The expression vector of claim 131, wherein said vector is suitable for transfection of a bacterial cell.

133. (currently amended) An isolated heterologous cell transfected with the vector of claim 130, wherein said cell expresses a biologically active  $\beta$ -secretase.

134. (previously presented) The cell of claim 133, wherein said cell is a eukaryotic cell.

135. (previously presented) The cell of claim 133, wherein said cell is a bacterial cell.

136. (previously presented) The cell of claim 133, wherein said cell is an insect cell.

137. (previously presented) The cell of claim 133, wherein said cell is a yeast cell.

138. (currently amended) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of, comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:67 or a perfectly complementary sequence thereof.

139. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 138 and a promoter, wherein the nucleic acid and the promoter are operably linked.

140. (previously presented) The expression vector of claim 139, wherein said vector is suitable for transfection of a bacterial cell.

141. (currently amended) An isolated heterologous cell transfected with the vector of claim 139, wherein said cell expresses a biologically active  $\beta$ -secretase.

142. (previously presented) The cell of claim 141, wherein said cell is a eukaryotic cell.

143. (previously presented) The cell of claim 141, wherein said cell is a bacterial cell.

144. (previously presented) The cell of claim 141, wherein said cell is an insect cell.

145. (previously presented) The cell of claim 141, wherein said cell is a yeast cell.

146. (previously presented) An isolated nucleic acid, comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 68 or a perfectly complementary sequence thereof.

147. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 146, and a promoter, wherein the nucleic acid and the promoter are operably linked.

148. (previously presented) The expression vector of claim 147, wherein said vector is suitable for transfection of a bacterial cell.

149. (currently amended) An isolated heterologous cell transfected with the vector of claim 147, wherein said cell expresses a biologically active  $\beta$ -secretase.

150. (previously presented) The cell of claim 149, wherein said cell is a eukaryotic cell.

151. (previously presented) The cell of claim 149, wherein said cell is a bacterial cell.
152. (previously presented) The cell of claim 149, wherein said cell is an insect cell.
153. (previously presented) The cell of claim 149, wherein said cell is a yeast cell.
154. (currently amended) An isolated nucleic acid encoding a beta secretase, the nucleic acid consisting of, comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 69 or a perfectly complementary sequence thereof.
155. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 154, and a promoter, wherein the nucleic acid and the promoter are operably linked.
156. (previously presented) The expression vector of claim 155, wherein said vector is suitable for transfection of a bacterial cell.
157. (previously presented) An isolated heterologous cell transfected with the vector of claim 155, wherein said cell expresses a biologically active  $\beta$ -secretase.
158. (previously presented) The cell of claim 157, wherein said cell is a eukaryotic cell.
159. (previously presented) The cell of claim 157, wherein said cell is a bacterial cell.



160. (previously presented) The cell of claim 157, wherein said cell is an insect cell.

161. (previously presented) The cell of claim 157, wherein said cell is a yeast cell.

162. (previously presented) An isolated nucleic acid, comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 70 or a perfectly complementary sequence thereof.

163. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 162, and a promoter, wherein the nucleic acid and the promoter are operably linked.

164. (previously presented) The expression vector of claim 162, wherein said vector is suitable for transfection of a bacterial cell.

165. (previously presented) An isolated heterologous cell transfected with the vector of claim 163, wherein said cell expresses a biologically active  $\beta$ -secretase.

166. (previously presented) The cell of claim 165, wherein said cell is a eukaryotic cell.

167. (previously presented) The cell of claim 165, wherein said cell is a bacterial cell.

168. (previously presented) The cell of claim 165, wherein said cell is an insect cell.

169. (previously presented) The cell of claim 165, wherein said cell is a yeast cell.

170. (previously presented) An isolated nucleic acid comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 74 or a perfectly complementary sequence thereof.

171. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 170, and a promoter, wherein the nucleic acid and the promoter are operably linked.

172. (previously presented) The expression vector of claim 171, wherein said vector is suitable for transfection of a bacterial cell.

173. (previously presented) An isolated heterologous cell transfected with the vector of claim 171, wherein said cell expresses a biologically active  $\beta$ -secretase.

174. (previously presented) The cell of claim 173, wherein said cell is a eukaryotic cell.

175. (previously presented) The cell of claim 173, wherein said cell is a bacterial cell.

176. (previously presented) The cell of claim 173, wherein said cell is an insect cell.

177. (previously presented) The cell of claim 173, wherein said cell is a yeast cell.

178. (previously presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 58 or a perfectly complementary sequence thereof conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

179. (previously presented) The method of claim 178, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

180. (previously presented) The method of claim 179, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

181. (previously presented) The method of claim 178, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

182. (previously presented) The method of claim 181, wherein said antibody binds specifically to SEQ ID NO: 58.

183. (Cancel)

184. (previously presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 59 or a perfectly complementary sequence thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

185. (previously presented) The method of claim 184, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

186. (previously presented) The method of claim 185, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

187. (previously presented) The method of claim 184, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

188. (previously presented) The method of claim 187, wherein said antibody binds specifically to SEQ ID NO: 59.

189. (cancel)

190. (currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 66 or a perfectly complementary sequence thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

191. (previously presented) The method of claim 190, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

192. (currently amended) The method of claim 191,[[,]] wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

193. (previously presented) The method of claim 190, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

194. (previously presented) The method of claim 193, wherein said antibody binds specifically to SEQ ID NO: 66.

195. (cancel)

196. (currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:67 or a perfectly complementary sequence thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

197. (previously presented) The method of claim 196, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

198. (previously presented) The method of claim 197, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

199. (previously presented) The method of claim 196, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

200. (previously presented) The method of claim 199, wherein said antibody binds specifically to SEQ ID NO: 67.

201. (cancel)

202. (previously presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 68 or a perfectly complementary sequence

thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

203. (previously presented) The method of claim 202, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

204. (previously presented) The method of claim 203, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

205. (previously presented) The method of claim 202, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

206. (currently amended) The method of claim 205,[[,]] wherein said antibody binds specifically to SEQ ID NO: 68.

207. (Cancel)

208. (currently amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:69 or a perfectly complementary sequence thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

209. (previously presented) The method of claim 208, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

210. (previously presented) The method of claim 209, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

211. (previously presented) The method of claim 210, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

212. (previously presented) The method of claim 208, wherein said antibody binds specifically to SEQ ID NO: 69.

213. (cancel)

214. (previously presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 70 or a perfectly complementary sequence thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

215. (previously presented) The method of claim 214, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

216. (previously presented) The method of claim 215, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

217. (previously presented) The method of claim 214, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

218. (previously presented) The method of claim 217, wherein said antibody binds specifically to SEQ ID NO: 70.

219. (cancel)

220. (previously presented) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 74 or a perfectly complementary sequence thereof under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

221. (previously presented) The method of claim 220, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

222 (previously presented) The method of claim 221, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

223. (previously presented) The method of claim 220, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

224. (previously presented) The method of claim 223, wherein said antibody binds specifically to SEQ ID NO: 74.

225. (cancel)

226. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

227. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

228. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.



229. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

230. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

231. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

232. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

233. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

234. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

235. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

236. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

237. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

238. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

239. (previously presented) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

240. (previously presented) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:58 or a perfectly complementary sequence thereof  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

241. (previously presented) The cell of claim 240, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

242. (previously presented) The cell of claim 240, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

243. (previously presented) The cell of claim 240, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

244. (previously presented) The cell of claim 240, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

245. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

246. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

247. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

248. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

249. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

250. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

251. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

252. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

253. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

254. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

255. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

256. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

257. (previously presented) The cell claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

258. (previously presented) The cell of claim 243, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

259. (previously presented) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:59 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

260. (previously presented) The cell of claim 259, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

261. (previously presented) The cell of claim 259, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

262. (previously presented) The cell of claim 259, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

263. (previously presented) The cell of claim 259, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

264. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

265. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

266. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

267. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

268. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

269. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

270. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

271. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

272. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

273. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

274. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

275. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

276. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

277. (previously presented) The cell of claim 262, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

278. (currently amended) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule comprising a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:66 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

279. (previously presented) The cell of claim 278, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

280. (previously presented) The cell of claim 278, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

281. (previously presented) The cell of claim 278, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

282. (previously presented) The cell of claim 278, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

283. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

284. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

285. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

286. (currently amended) The cell of claim 281,[[,]] wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

287. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

288. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

289. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

290. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

291. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

292. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

293. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

294. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

295. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.



296. (previously presented) The cell of claim 281, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

297. (currently amended) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule encoding a beta secretase, the nucleic acid consisting of  
~~comprising~~ a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:67 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

298. (previously presented) The cell of claim 297, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

299. (previously presented) The cell of claim 297, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

300. (previously presented) The cell of claim 297, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

301. (previously presented) The cell of claim 297, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

302. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

303. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

304.[[.]] (currently amended) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

305.[[.]] (currently amended) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

306. (currently amended) The cell of claim 300,[[.]] wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

307. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

308. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

309. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

310. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

311. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

312. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

313. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

314. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

315. (previously presented) The cell of claim 300, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

316. (previously presented) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:68 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

317. (previously presented) The cell of claim 316, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

318. (previously presented) The cell of claim 316, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

319. (previously presented) The cell of claim 316, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

320. (previously presented) The cell of claim 316, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

321. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

322. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

323. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

324. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

325. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

326. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

327. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

328. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

329. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

330. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

331. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

332. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

333. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

334. (previously presented) The cell of claim 319, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

335. (currently amended) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:69 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

336. (previously presented) The cell of claim 335, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

337. (previously presented) The cell of claim 335, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

338. (previously presented) The cell of claim 335, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

339. (previously presented) The cell of claim 335, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

340. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

341. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

342. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

343. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

344. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

345. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

346. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

347. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

348. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

349. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

350. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

351. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

]352. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

353. (previously presented) The cell of claim 338, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

354. (Currently amended) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:70 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

355. (previously presented) The cell of claim 354, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

356. (previously presented) The cell of claim 354, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

357. (previously presented) The cell of claim 354, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

358. (previously presented) The cell of claim 354, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).



359. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

360. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

361. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

362. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

363. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

364. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

365. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

366. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

367. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

368. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

369. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

370. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

371. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

372. (previously presented) The cell of claim 357, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

373. (currently amended) An isolated heterologous cell, comprising  
(i) a nucleic acid molecule comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:74 or a perfectly complementary sequence thereof;  
(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and  
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

374. (previously presented) The cell of claim 373, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

375. (previously presented) The cell of claim 373, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

376. (previously presented) The cell of claim 373, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

377. (previously presented) The cell of claim 373, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

378. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

379. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

380. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

381. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

382. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

383. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

384. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

385. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

386. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

387. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

388. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

389. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

390. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

391. (previously presented) The cell of claim 376, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.